# Pediatric acute-onset neuropsychiatric syndrome in a 6.5-year-old boy: A case report

*Case Report*

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## Abstract

***Background:*** "Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections", or PANDAS, is a syndrome characterized by acute-onset obsessive-compulsive disorder (OCD) and/or tics accompanied by the neuropsychiatric symptoms. This case is reported because of its rarity.

***Case report:*** A 6.5-year-old boy with swollen tonsils, high-grade fever and rash was admitted to Amirkola Children's Hospital, Northern Iran. Thereafter he got involved with tachycardia, hypotension, suppurative conjunctivitis and swelling of extensor surfaces of extremities. In addition, after the onset of fever, he had some neuropsychiatric problems such as social isolation, irritability, aggression, oppositional behavior, behavioral regress, unusual sound production, repeated vilifications, loss of appetite and handwriting deterioration. He was treated with intravenous immunoglobulin (IVIG). The patient was discharged from the hospital in a good condition.

***Conclusions:*** The medical treatment of underlying disease leads to remarkable patient's neuropsychological and OCD symptoms. PANDAS should be diagnosed in the streptococcal infections associated with abrupt behavioral symptoms and treated with IVIG and antibiotics.

***Key Words:*** Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections, Pediatric, Autoimmune diseases, IVIG

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## Introduction

The term "pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections" or PANDAS was created by Swedo et al. [1] who defined it as a subset of childhood obsessive-compulsive disorder (OCD) and tic disorders triggered by group A beta-hemolytic streptococcal (GABHS) infection [2]. There are five clinical criteria including neurological abnormalities, acute onset and relapsing-remitting course, group A streptococcal (GAS) infection, prepubertal onset and presence of OCD or tic disorder to differentiate PANDAS subgroup from other cases of childhood-onset OCD [1]. Though many literatures stated strong evidence for the distinctive laboratory and clinical presentation of the PANDAS subgroup, other articles marked the diagnosis ''controversial'' as well as investigated the nature assumed etiology and even the existence of PANDAS [3-6]. Certain criticism was arisen around the requirement that the symptoms temporally related to GAS infections have an acute episodic/onset course since their operationalizing is difficult in community settings [6, 7]. Presently, the most broadly accepted hypothesis suggests that the antineuronal antibodies, leading to manifestation of motor and behavioral disturbances are caused by an autoimmune poststreptococcal process in susceptible children [8, 9]. PANDAS may be distinguishable from non-PANDAS OCD via specifications associated with basal

ganglia functions such as deterioration in handwriting, impulsivity, urinary urgency and hyperactivity [1]. The excellent response of children with PANDAS to immunotherapies such as intravenous immunoglobulin (IVIG) and plasma exchange (PE) proves the autoimmune mediated mechanism [10]. We decided to argue about psychological problems probably due to the microbial reason which can be treated medically, with treatment of background etiology. The correlation of medical treatment of an infectious disease and neuropsychologic improvement is one of the novel issues of the recent years.

## Case presentation

A 6.5-year-old boy with a 3-day history of swollen tonsils, sore throat, exfoliative lips, rhinorrhea, epistaxis, high-grade fever, chills and rash was admitted to Amirkola Children's Hospital. The nonpruritic rash first appeared on his abdomen, chest and back then spread to his arms, legs and face. He had no known history of allergies or exposures to new medications and had no history of similar rash. Examination revealed exudative tonsillitis, strawberry tongue and cervical lymphadenopathy with tenderness as well as the skin examination indicated diffuse blanching erythema. During the hospitalization, he got involved with tachycardia, hypotension, suppurative conjunctivitis, swelling of extensor surfaces of extremities. In addition, he had some neuropsychiatric problems such as social isolation at the first day of recent illness, irritability, aggression, oppositional behavior, behavioral regress, unusual sound production, repeated vilifications, loss of appetite and handwriting deterioration after the onset of fever. Antistreptolysin O (ASO) titer test was negative but C-reactive protein (CRP) was at a high level. At first, the clinical findings including acute streptococcal pharyngitis along with the diffuse rash led us to a diagnosis of toxic shock syndrome, but after admission, the neuropsychiatric symptoms such as exacerbated aggressiveness and irritability led us to a diagnosis of PANDAS. The patient was treated with antibiotic agents and IVIG. Surprisingly, his irritability, aggression, oppositional behaviors, repeated vilifications and anorexia disappeared immediately after IVIG transfusion and the patient had complete resolution of rash within 3 days.

In past psychological history, he was suffering from OCD, separation anxiety, emotional lability and depression, sleep disturbances like nightmares in addition to early and late insomnia, urinary frequency as well as death and injection phobia from long time ago. Sydenham's chorea did not exist in the history. In addition, it should be noted that his father and brother had a history of untreated attention deficit hyperactivity disorder and conduct disorder.

## Discussion

This case report has described a patient with abrupt onset of tic, loss of appetite, fever and rash in the context of chronic OCD such as aggressive or horrific thoughts about harming himself or others as an obsessive behavior and silently repetition of a prayer, word or phrase as a compulsive behavior, previous history of anxiety, emotional lability, depression, oppositional behavior and urinary frequency. It seems that the current illness temporally relates to GABHS infection. High intensity neuropsychiatric symptoms, typical clinical manifestations and remarkable improvement with IVIG encouraged us to report this case.

Pediatric acute-onset neuropsychiatric syndrome (PANS) is characterized by the dramatic and abrupt onset of OCD and/or severely restrictive food intake with at least two concurring equally debilitating symptoms including irritability/ aggression/ oppositionality, mood dysregulation, anxiety, cognitive deterioration, somatic symptoms sensory or motor abnormalities and behavioral regression consisting of vilifications, poor nonverbal and verbal communication skills and nonsense speech [11]. It is supposed that the syndrome originates from various disease mechanisms and has different etiologies, ranging from psychological trauma or underlying neurological, endocrine and metabolic disorders to postinfectious autoimmune and neuroinflammatory disorders like PANDAS, and other infectious agents such as varicella and rickettsia, herpes, neuropsychiatric lupus, cerebral vasculitis and others since the PANS criteria describe a broad spectrum of neuropsychiatric conditions [12]. When the onset of flares is related to GAS, the disorder is called PANDAS, a syndrome which is specified by acute-onset OCD and/or tics besides the neuropsychiatric symptoms as mentioned earlier [1, 11].

It has found that almost 20% of PANS cases cannot fulfill the PANDAS criteria for there is no documentation of GAS infections [6].

Our patient met PANDAS criteria confirmed by a pediatric psychiatrist. PANDAS is known by five clinical characteristics and one of them is a distinct

association with GABHS infection [1]. The most commonly used antibody determinations are tests applied for antibodies against DNAse B (anti–DNAse B) and streptolysin O (ASO) while sometimes it is necessary to assess other streptococcal antibodies [13]. Our patient had a negative ASO titer test result initially but then it was raised to higher than 200 IU.

Since the suggested autoimmune mechanism is the same as that of Sydenham's chorea, it has resulted in experimental trials with prophylactic antibiotics and immunomodulatory agents consisting of IVIG and PE [8, 9]. Perlmutter et al. successfully used both IVIG and PE to reduce symptom frequency in patients who fulfilled the PANDAS diagnostic criteria [8, 9]. However, the use of this treatment modality has not been broadly accepted because the immunomodulatory therapies carry remarkable morbidity and the study has not been replicated.

In May 2014, at a meeting held at the National Institutes of Health in Bethesda, Maryland, the members of the PANS/PANDAS Research Consortium (PRC) started the development of the treatment guidelines. Two years later, three workgroups made modifications and refinements, and separately addressed (a) the use of antimicrobials, (b) the use of immunomodulating and anti-inflammatory therapies, and (c) the use of behavioral interventions and psychiatric medications [12].

Thus, some researchers have proposed the cognitive-based therapy, selective serotonin reuptake inhibitors along with the antibiotic treatment for GABHS infections with standard pharmacologic and nonpharmacologic treatment of tic disorder or persistent OCD symptoms [8, 14]. However, Miro Kovacevic et al. observed that all patients had failed prior therapies and stated that the immunomodulatory effects of IVIG were responsible for the symptomatic improvements [15].

Appropriate response to antibiotic therapy and IVIG was found in our patient. Six months after discharge, he was examined again at an outpatient clinic and it was seen that his mood and behavior were normal as well as no sign and symptom of PANDAS was observed.

In conclusion, the PANS can be correlated with several years of abnormal behaviors involving emotional lability, anxiety, enuresis and other neuropsychiatric symptoms. In this case report, IVIG therapy appeared to provide the best results; but in the case of eradicating the infectious etiologic agent, antibiotic therapy seemed necessary, too. This case report emphasizes the diagnosis of PANDAS in a patient with streptococcal infection associated with the abrupt behavioral symptoms and considers IVIG along with the etiologic treatment for infection as an effective therapy.

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